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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/067,484	02/04/2002	Bob B. Buchanan	416272000200	7171

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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 05/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/067,484	BUCHANAN ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,16-18,22-24,32-35 and 47-51* is/are pending in the application.

4a) Of the above claim(s) *47,49 and 50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,14,16-18,22-24,32-35,48 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Please note that the examiner of record for your application has changed. To aid in paper matching, please address all future correspondence to Michael Szperka, Art Unit 1644, Technology Center 1600.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 23, 2006 has been entered.

Applicant's response, amendments and declaration received October 24, 2005 and February 23, 2006 are acknowledged.

Claims 4-13, 15, 19-21, 25-31, 36-46 have been canceled.
Claims 1, 32, and 48 have been amended.
Claims 1-3, 14, 16-18, 22-24, 32-35, 47-51 are pending.
Claims 47, 49, and 50 stand withdrawn for the reasons of record as being drawn to non-elected inventions.
Claims 1-3, 14, 16-18, 22-24, 32-35, 48, and 51 are under examination as they read on isolated ragweed allergens, compositions comprising said allergens, and kits comprising said allergens.

2. The declaration of Bob B. Buchanan under CFR 1.132 stating that Suzanne Teuber did not make any original contribution to the work described in del Val et al. (reference 6 on the IDS received 2/3/03, or record, see entire document) relevant to what is claimed in the instant application is acknowledged.

In light of this declaration and the earlier declaration by Bob B. Buchanan under CFR 1.132 received June 7 2006 that Joshua Wong did not make any independent contribution work described in the article by del Val et al., the teachings of the del Val et al. reference no longer discloses the work of an inventive entity distinct from the instant inventors. As such, the rejection of record of claims 1-3, 14, 16-18, 22-24, 48, and 51 under 35 USC 102(a) has been withdrawn.

3. On page 3 of the office action mailed March 1, 2005, it was indicated that provisional application 60/266,686 filed February 5, 2001 disclosed the sequences of SEQ ID NOs:1-5 but did not disclose other sequences found in the instant specification such as SEQ ID NOs:6-11. The claims as amended February 23, 2006 have been amended to recite only the peptide sequences of SEQ ID NO:1-5 by deleting SEQ ID NOs:6-11 from the claimed invention, and thus the instant claimed invention has support in the '686 provisional application. As such, the rejection of claims 1-3, 14, 16-18, 22-24, 48, and 51 under 35 USC 102(b) has been withdrawn since the del Val et al. reference was not publicly available more than one year prior to the February 5, 2001, the date on which the '686 provisional application was filed.

Declarations under CFR 1.131 have also been submitted February 23, 2006 by inventors Buchanan, del Val, and Frick to establish that the instant claimed subject matter was reduced to practice prior to February 1, 2001 and thus antedate the reference of del Val et al. As was explained above, the del Val et al. reference no longer qualifies as art under 35 USC 102(a) and the rejection under 35 USC 102(b) has been removed because the instant claimed subject matter is disclosed in provisional application 60/266,686 filed February 5, 2001. As such, the declarations have not been further considered.

4. The rejection of record under 35 USC 103(a) of claims 32-35 as unpatentable over del Val et al. in view of US Patent No. 4,281,061 has been withdrawn since applicant has demonstrated that the del Val et al. reference does not qualify as prior art for the reasons discussed above.

5. Applicant has successfully removed all outstanding objections and rejections of record. Upon reconsideration of the claimed subject matter, the following new grounds of rejection have been set forth:

Claim Objections

Claims 22, and 32 are objected to because they recite "Ambt7" the proper nomenclature for allergens as per the WHO/IUIS guidelines would be Amb t 7, as appears for instance in paragraph 196 on page 67 of the instant specification. Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 14, 16-18, 32-35, 48, and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 14 and 16-18 are indefinite because while the independent claim recites protein and peptide fragments thereof, the recited structural and functional properties cannot pertain to the recited fragments. Additionally, the dependent claims recite "the allergen of claim 14" yet the preamble of claim 14 recites pollen protein or fragment thereof and as such this terminology lacks proper antecedent basis. Further, the size of the peptide fragments of claim 14 are not recited and it is well known that for antigens to act as allergens, they must elicit T-cell-dependent responses and contain at least two, and preferably 3 or 4 spatially separated epitopes in addition to interacting specifically with IgE, that epitopes are generally about 13 amino acids in length, and that an antigen, such as a peptide fragment, cannot be distinguished as allergic or nonallergic on an a priori structural basis (Blumenthal et al. in Allergens and Allergen Immunotherapy, third edition, 2004, pages 37-50, see entire document, particularly the second full paragraph of page 38, the last sentence of the third full paragraph of page 39, and the first sentence of the first full

paragraph of page 42, and Goldsby et al., Immunology, fifth edition, 2004, pages 62-68, see entire document, particularly the right column of page 68). As such the metes and bound of the peptide fragments recited in the claims are not known. Similarly, dependent claims 48 and 51 recite multiple structural and functional properties that are not present in the peptides recited by SEQ ID number in the instant claims.

Claims 32-35 are indefinite because independent claim 32 recites a kit for detecting one or more ragweed proteins wherein the one or more proteins comprise an amino acid sequence selected from the group consisting of SEQ ID NOs:1-5, yet the specification discloses that the peptides of SEQ ID NO:1-5 are all part of the same allergen, namely the 30 kDa Amb t 7 ragweed pollen allergen (see particularly paragraph 6 on page 2 and paragraphs 183-197, pages 66-68). What other ragweed allergen(s) are being detected?

Further, claim 34 recites a kit including antibodies, but the antigen specificity of the antibodies included as part of the kit is not specified. Do the antibodies specifically bind ragweed pollen antigens, human IgE, or something else? As such, the metes and bounds of the instant claimed kit are not known.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-3, 14, 16-18, 22-24, 32-35, 48, and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant has claimed a genus comprising an isolated ragweed pollen protein that comprises recited biophysical properties including its presence in pollen extracts as a 30,000 Dalton (30 kDa) glycoprotein that contains sulfhydral groups and acts as an allergen, as well as fragments of said protein, when these products are present by themselves or when they comprise

a pharmaceutical composition or kit. To support this genus applicant has disclosed the 30 kDa protein and the fragments of SEQ ID NOs:1-5. This disclosure does not support the claimed genus for the following reasons:

The claimed full length protein is recited as having specific structural and functional properties, but these properties such as apparent molecular weight and allergenicity do not convey to the claimed fragments of the 30 kDa protein, including the fragments of SEQ ID NOs:1-5 that range from 7 to 14 amino acids in length. The peptides of SEQ ID NOs:1-5 are disclosed as being obtained by mass spectroscopy following trypsin digestion of the 30 kDa protein of the instant invention (see particularly pages 66 and 67 of the specification). The specification does not appear to teach that the peptides of SEQ ID NOs:1-5 have any particular functional activity, such as being B or T cell epitopes as is recited in dependent claims 23 and 24, or being allergens as is recited in independent claim 32 and dependent claims 16-18, 33-35. Note that the fragments recited independent claims 1 and 14 and dependent claims 2, 3, 48 and 51 do not appear to have any recited functional activities.

It is known in the art that for antigens to act as allergens, they must elicit T-cell-dependent responses and contain at least two, and preferably 3 or 4 spatially separated epitopes in addition to interacting specifically with IgE, and that an antigen cannot be distinguished as allergic or nonallergic on an a priori structural basis (Blumenthal et al. in Allergens and Allergen Immunotherapy, third edition, 2004, pages 37-50, see entire document, particularly the second full paragraph of page 38, the last sentence of the third full paragraph of page 39, and the first sentence of the first full paragraph of page 42). Applicant has provided data that the 30 kDa protein is recognized as a human allergen (see particularly pages 63-66 and Figures 5-7) and teaches that it can be used to induce an allergic response in an atopic dog model system (see particularly pages 66 and 67 of the specification). No data or teachings concerning the structure of the protein that is required for its allergenicity or of the identity of the allergenic epitopes present in the protein that are recognized by the immune system appears to be disclosed in the instant specification, and as such it does not appear that a skilled artisan would be able to recognize fragments of the 30 kDa protein that maintain the disclosed functional property of being an allergen.

The guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 column 3). As discussed above, the domains or regions of the claimed fragments of the 30 kDa protein, whether or not recited as comprising a peptide of SEQ ID NOs:1-5, do not appear to have a structure defined by the specification that must be maintained for functional activity of being an allergen and the specification does not appear to disclose other functional activities that correlate with the structure of being a polypeptide that comprises a sequence selected from the group consisting of SEQ ID NOs:1-5. In light of this, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus of fragments of the isolated 30 kDa protein of the instant invention.

10. Claims 1-3, 14, 16-18, 22-24, 32-35, 48, and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated ragweed pollen glycoprotein allergen that is about 30,000 Daltons (30 kDa) as measured by SDS-PAGE, contains sulfhydral groups, and comprises the peptides of SEQ ID NO:1, 2, 3, 4 and 5, does not reasonably provide enablement for peptide fragments of said ragweed allergen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant teaches the isolation of a 30 kDa allergen from ragweed pollen that contains carbohydrate and sulfhydral groups and comprises all of the tryptic peptides of SEQ ID NOs:1-5. Applicant's claims are broader than this in that the recited invention also includes fragments of the isolated 30 kDa allergen. Note that the claimed fragments need not comprise any disclosed sequence (such as in independent claim 14) or the claimed fragments may comprise one, but not

necessarily all, of the peptides of SEQ ID NOs:1-5 as is recited, for example, in independent claim 1. The specification teaches that the peptides of SEQ ID NOs:1-5 were obtained by digestion of the 30 kDa allergen with trypsin followed by mass spectroscopy, and as such these sequences are all part of the primary amino acid sequence of the 30 kDa allergen (see particularly pages 66 and 67). The specification does not teach the full length sequence of the 30 kDa allergen. The specification provides guidance and working examples concerning the use of the 30 kDa allergen in pharmaceutical and diagnostic compositions for the diagnosis and treatment of allergy in humans and dogs (see particularly pages 46-52, 63-68, and Figures 5-7). The specification also teaches that fragments of the 30 kDa ragweed allergen can be administered to patients to treat ragweed allergies because they contain B cell epitopes, T cell epitopes, or both B and T cell epitopes (see particularly pages 18 and 19, most particularly paragraph 71 on page 18). The identity of the B and T cell epitopes found within the 30 kDa ragweed allergen are not taught, and the tryptic peptide fragments of SEQ ID NOs:1-5 are not taught as being recognized by B or T cells.

It is known in the art that for antigens to act as allergens, they must elicit T-cell-dependent responses and contain at least two, and preferably 3 or 4 spatially separated epitopes in addition to interacting specifically with IgE, and that an antigen cannot be distinguished as allergic or nonallergic on an a priori structural basis (Blumenthal et al. in Allergens and Allergen Immunotherapy, third edition, 2004, pages 37-50, see entire document, particularly the second full paragraph of page 38, the last sentence of the third full paragraph of page 39, and the first sentence of the first full paragraph of page 42). It is also known that B cell epitopes (i.e. those recognized by antibodies) come in two types, linear and discontinuous (Goldsby et al., Immunology, fifth edition 2003, pages 62-67, see entire selection). Discontinuous epitopes are made up of amino acids that are close together in the native tertiary structure of an antigen but are far apart in the primary amino acid sequence, and antibodies typically contact 15-22 amino acids in binding to an epitope (Goldsby et al., see particularly pages 63 and 64). The majority of B cell epitopes present on allergens are of the discontinuous type, such epitopes being dependent upon the native conformation of the protein (King et al., J Immunology, 2001, 166:6057-6065, see entire document, particularly the second paragraph of the left column of page 6057 and the last sentence of the paragraph that spans pages 6063 and 6064). As such, it appears reasonable

that the claimed genus of fragments of the 30 kDa ragweed allergen are not all allergens since this genus reads on small fragments (including peptides that consist of the 7 to 14 amino acids of SEQ ID NOs:1-5) that do not comprise two or more spatially separated epitopes due to their small size and that such small fragments are unlikely to be B cell epitopes since their small size does not allow for the presence of discontinuous epitopes.

T cell epitopes are more complicated than B cell epitopes in that for a T cell epitope to be recognized it must be proteolytically processed from a larger polypeptide and then presented in an appropriate MHC molecule for inspection by T cell of the vertebrate immune system (Goldsby et al., Immunology, fifth edition, see particularly pages 67-68). The specification does not appear to provide specific guidance concerning how to identify T cell epitopes of the 30 kDa ragweed allergen, and it is known in the art that predictions concerning peptide binding to MHC molecules are often wrong, and if the peptide cannot be bound and presented by an MHC molecule it cannot effectively serve as a T cell epitope (Goulmy et al., US 2004/0092446, see entire document, particularly Example 3 and most particularly paragraph 168). Given that an individual expresses only a limited number of MHC molecules and given that any one particular peptide epitope is unlikely to be bound by an MHC molecule found in every member of the population (Janeway et al., Immunobiology, third edition 1999, pages 4:24-4:30, see entire selection) it is difficult to define T cell epitopes without consideration of the MHC haplotypes of the intended patient population; but neither the specification or the instant claims appear to provide guidance concerning the resolution of these issues. Notably, neither the specification nor the instant claims provide guidance or recitation as to the structure(s) of the instant claimed peptide fragments that give rise to the above discussed biological activities and therefore must be maintained in a peptide fragment of the instant invention, or conversely, what is not important for the above discussed biological activities and can thus be left out of the claimed peptide fragments. Note that the 30 kDa allergen protein is a full length protein and as such it should contain multiple T and B cell epitopes, as is evidenced by the recognition of the full length 30 kDa ragweed protein as an allergen in humans and dogs as was discussed above.

Therefore, given the breadth of applicant's claims which read on fragments of the 30 kDa ragweed allergen of the instant invention, the art recognized difficulties in determining B and T cell peptide epitopes, the lack of guidance, direction and working examples concerning peptide

fragments of the 30 kDa ragweed allergen that contain B or T cell epitopes, and the apparent lack of a disclosed use for peptide fragments of the 30 kDa ragweed allergen that do not comprise B or T cell epitopes, a skilled artisan would not be able to make and use the full breadth of applicant's claimed invention without conducting an undue amount of additional research.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 14, 16, 17, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by King et al. (Biochemistry, 1967, 6:1992-2000, see entire document).

King et al. teach the isolation of an allergen from ragweed pollen that has an apparent molecular weight of 38,200 Daltons, comprises sulfhydral groups, and comprises carbohydrate thus making it a glycoprotein (see entire document, particularly the abstract, the paragraph spanning pages 1994-1995, and Table II). This purified allergen was used in pharmaceutical compositions to immunize rabbits for the production of allergen-specific antibodies (see particularly the middle of the right column of page 1992, Table III, and Figure 7) and was used as a diagnostic composition to conduct skin tests in patients (see particularly the paragraph spanning the left and right columns of page 1996 and Figure 6).

It is noted that the instant claims recite an apparent molecular weight of "about 30,000." The specification does not appear to define the range of values encompassed by the limitation "about", and as such the 38,200 Dalton protein of King et al. is about 30,000 Daltons.

Therefore, the prior art anticipates the claimed invention.

13. No claims are allowable.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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May 9, 2006

5/15/06
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